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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,328	02/12/2002	Jeff Steven Grotelueschen Hall	FORS-06930	5712

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EXAMINER	
SITTON, JEHANNE SOUAYA	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/074,328	GROTELUESCHEN HALL ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *101-107,109 and 111-125* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *101-107, 109, 111-125* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 101-107, 109 and 111-125 are pending in the instant application. Claims 108 and 110 have been canceled. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are newly applied to the amended claims, as necessitated by amendment, or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection of claims 101-125 made under 35 USC 112/2nd paragraph at section 5 of the previous office action is moot in view of the amendments to claims 101 and 113.

4. The rejection of claims 101-103 and 105-125 made under 35 USC 112/1st paragraph at section 6 of the previous office action is moot in view of the amendment to recite "set of reagents" instead of "kit".

Maintained Rejections

5. Claim 104 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

The rejection of claim 104 made at section 6 of the previous office action is maintained and reiterated herein. The response asserts that the claims have been amended, however claim 104 continues to recite "kit".

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claim 104 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 104 lacks antecedent basis for the recitation of "kit".

Claim Rejections - 35 USC § 102

7. Claims 101-104, 107, 109, 111-112, 114-117, and 123-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Lyamichev et al (hereinafter referred to as Lyamichev; Science, vol. 260, May 1993, pages 778-782).

Lyamichev teaches a composition comprising 1) a cleavage agent (polymerase) which is a thermostable (stable at a specific temperature, cleaves at 72 deg. C) structure specific nuclease which comprises a thermostable 5' nuclease (DNAP-Taq, which has a portion of the amino acid sequence of the nuclease is homologous to a portion of the amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism) (claims 107-109, 111; see Fig. 1); 2) a buffer solution (page 783, note "5"; instant claim 112); 3) a first oligonucleotide

comprising a charged adduct (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group) and a portion completely complementary to a first region of a target nucleic acid, 4) a second oligonucleotide comprising a 3' portion and a 5' portion, said 5' portion completely complementary to a second region of said target nucleic acid downstream of and contiguous to said first region; and 5) a target nucleic acid, (see figure 6; instant claim 114). It is noted that the cleaved nucleic acid can be considered the second oligonucleotide and the uncleaved portion can be considered the first oligonucleotide. As such, with regard to claims 102 and 103, wherein the cleaved nucleic acid is interpreted as the 2nd oligonucleotide, Lyamichev teaches that the 2nd oligonucleotide comprises and consists of a single nucleotide not complementary to the target.

It is noted that the method of Lyamichev utilizes more than one template strand in each reaction. As the claims do not make clear that the first target and the second target are different, such teaching is interpreted to encompass instant claim 115.

With regard to claim 116, the claim sets forth no structural limitations for "linker". Therefore, the recitation of "linker" has been given its broadest reasonable meaning which encompasses the sugar group of the nucleotide.

With regard to claim 117, Lyamichev teaches that the 5' arm which is cleaved (the first oligonucleotide) comprises a label which is detectable (see figure 2; instant claims 117 and 123).

With regard to claims 124 and 125, Lyamichev teaches that only certain regions are cleaved in the first oligonucleotide, therefore Lyamichev inherently teaches that the first oligonucleotide comprises an uncleavable region which is attached to the charged adduct.

With regard to claim 104, Lyamichev teaches resolving the components of the reaction on a gel, which is a "solid support".

Response to Arguments

8. The response traverses the rejection. The response at page 7, para 1, gives a brief overview of the invention. It is noted, however, that the response lists limitations in such paragraph, that are not recited in the claims. For example, the response asserts that "when the nucleic acids are annealed in this fashion, the 3' portion of the 2nd nucleic acid molecule overlaps with the duplex formed by the first nucleic acid molecule and the target nucleic acid". Additionally, the response asserts "When aligned with the target... the first and second nucleic acid molecules can anneal to the target such that the contiguous first and second regions of the target are both completely annealed to form contiguous duplexes". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a second oligonucleotide with a 3' portion that can overlap with the substrate duplex, first and second regions completely annealed) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The instant claims encompass at the very least 3 nucleic acids, wherein two of the nucleic acids possess a 'portion' (which can be 1 nucleotide) that are completely complementary to regions of the target. Additionally, the target need only possess 2 regions which are contiguous to each other which is taught by Lyamichev. The claims are drawn only to a set of reagents, they are not drawn to a method requiring a target and

oligonucleotides hybridized to each other in a specific orientation, or to any specific structure formed by a target and oligonucleotides. These reagents can be nucleic acids and a "cleavage agent" before or after a reaction has taken place.

At paragraph 2, the response asserts that Lyamichev fails to teach or suggest reagents comprising first and second oligonucleotides that anneal to contiguous regions of a target nucleic acid, wherein the second oligonucleotide further comprises a 3' portion. This argument has been thoroughly reviewed but was not found persuasive as the structures of the 2nd oligonucleotide referenced above contain a 3' portion. Again, it should be noted that these claims are not limited to a specific structure comprised of a target and oligonucleotides annealed to such. They are only drawn to a set of reagents that have specific structural features, which are taught by Lyamichev. The argument that Lyamichev does not teach or suggest primers that additionally comprise a 3' portion that can overlap with the substrate duplex is not found persuasive for the reasons made of record above. It should additionally be noted that the terms "3' portion", and "5' portion" have not been interpreted to be limited to 3' or 5' termini, respectively, of a molecule. A portion can be considered a "3'" portion as long as it has something 5' to it, even a single nucleotide, and vice versa. Therefore, any sequence inherently has a 3' portion and a 5' portion.

9. Claims 101, 112-115, 117, 118 and 123 are rejected under 35 U.S.C. 102(b) as being anticipated by Livak et al (hereinafter referred to as Livak; PCR methods and applications, vol. 4, pages 357-362, June 1995).

Livak discloses a composition comprising 3 oligonucleotides (a probe and 2 primers) and Taq polymerase (cleavage agent) in a buffer solution, wherein the probe is labeled with a fluorescent dye at its 5' end (charged adduct) (instant claims 101, 112, 113, 117, and 118). It is further noted that any of the nucleotides at the 5' end of any of the oligonucleotides can also be considered a "charged adduct" (claim 123).

Response to Arguments

10. The response traverses the rejection and asserts that Livak fail to teach reagents comprising first and second oligonucleotides that can anneal to contiguous regions of a target wherein the 2nd oligonucleotide further comprises a 3' portion. This argument has been thoroughly reviewed but was found unpersuasive. The claims only require that a target nucleic contain two contiguous regions, it is not limited to a structure where 2 oligonucleotides are hybridized contiguous to each other, or to oligonucleotides that hybridize over a complete region of the target. Further, the term "region" is not specifically defined, and it is not clear how many nucleotides are necessary to define a "region" on the target. Two nucleotides side by side would encompass a first region contiguous to a second region. It should additionally be noted that the terms "3' portion", and "5' portion" have not been interpreted to be limited to 3' or 5' termini, respectively, of a molecule. A portion can be considered a "3'" portion as long as it has something 5' to it, even a single nucleotide, and vice versa. Therefore, any sequence inherently has a 3' portion and a 5' portion. Even so, the sequences of Livak have 3' termini.

11. Claims 101, 104-107, 114-119, and 122-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Urdea (US Patent 5,380,833; 1/10/1995).

Urdea teaches a reaction comprising a thermostable cleavage agent (col. 20) a first oligonucleotide and a 2nd oligonucleotide hybridizable to a target sequence (see figure 2B(a); instant claim 101). It is noted that the term 'cleavage agent' has not been defined by the specification (the specification only defines a 'cleavage means'). As such the term has been broadly interpreted to encompass a reagent used with something that has cleavage activity, such as a salt composition [which is inherently thermostable, that is stable at a specific temperature (the specification does not limit the term to any specific temperature)] which comprises (contains) a restriction enzyme (see col. 20, lines 34-35). Urdea teaches that both oligonucleotides are "attached" to the solid support (instant claims 104-106). The term "structure specific" nuclease is not defined by the specification. Therefore the recitation has been broadly interpreted to encompass a restriction enzyme (claim 107). Urdea teaches that labels include fluorescein (see col. 7, lines 36-65; instant claims 117-119). Urdea also teaches a charged adduct that comprises an amino-modified base (see col.22, lines 18-40 and col. 24, lines 21-65, instant claim 122). As the claims do not make clear that the first target and the second target are different, such teaching of more than one target in a reaction is interpreted to encompass instant claim 115.

Response to Arguments

12. The response traverses the rejection and asserts that Urdea fails to teach reagents comprising first and second oligonucleotides that can anneal to contiguous regions of a target

wherein the 2nd oligonucleotide further comprises a 3' portion. This argument has been thoroughly reviewed but was found unpersuasive. The claims only require that a target nucleic contain two contiguous regions, it is not limited to a structure where 2 oligonucleotides are hybridized contiguous to each other, or to oligonucleotides that hybridize over a complete region of the target. Further, the term "region" is not specifically defined, and it is not clear how many nucleotides are necessary to define a "region" on the target. Two nucleotides side by side would encompass a first region contiguous to a second region. It should additionally be noted that the terms "3' portion", and "5' portion" have not been interpreted to be limited to 3' or 5' termini, respectively, of a molecule. A portion can be considered a 3' portion as long as it has something 5' to it, even a single nucleotide, and vice versa. Therefore, any sequence inherently has a 3' portion and a 5' portion. Even so, the sequences of Urdea have 3' termini.

13. Claims 101, 107, 112, 114-116, 120, 121, and 123-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Corey (J. Am. Chem. Soc, 1995, vol. 117, pages 9373-9374).

Corey teaches a composition comprising 2 oligonucleotides (the first oligonucleotide: primer comprising amino acids at 5' end, 2nd oligonucleotide: one of the strands of DNA template; see figure 1a) and a thermostable cleavage agent (see page 9373, 2nd col 2, 2nd para; page 9374, col. 2, first full para). It is noted that the term 'cleavage agent' has not been defined by the specification (the specification only defines a 'cleavage means'). As such the term has been broadly interpreted to encompass a reagent used with something that has cleavage activity, such as a salt composition [which is inherently thermostable, that is stable at a specific

temperature (the specification does not limit the term to any specific temperature)] which comprises (contains) a polymerase with nuclease activity. Corey teaches that the first oligonucleotide is modified at it's 5' end with a charged adduct (Lysine or arginine amino acid, see table 1; instant claims 101, 112, 120, 121, and 123). Further, Corey inherently teaches that the first oligonucleotide comprises an uncleavable region which is attached to the charged adduct because neither the adduct nor the first oligonucleotide are cleaved in the reaction of Corey (instant claims 124-125). The composition of Corey comprises the more than one copy of the target (instant claim 115). Further, the term "linker" in claim 116 has been broadly interpreted to encompass any of the molecules between the 5' most lysine and the primer.

Response to Arguments

14. The response traverses the rejection and asserts that Corey fails to teach reagents comprising first and second oligonucleotides that can anneal to contiguous regions of a target wherein the 2nd oligonucleotide further comprises a 3' portion. This argument has been thoroughly reviewed but was found unpersuasive. The claims only require that a target nucleic contain two contiguous regions, it is not limited to a structure where 2 oligonucleotides are hybridized contiguous to each other, or to oligonucleotides that hybridize over a complete region of the target. Further, the term "region" is not specifically defined, and it is not clear how many nucleotides are necessary to define a "region" on the target. Two nucleotides side by side would encompass a first region contiguous to a second region. It should additionally be noted that the terms "3' portion", and "5' portion" have not been interpreted to be limited to 3' or 5' termini, respectively, of a molecule. A portion can be considered a 3' portion as long as it has something

5' to it, even a single nucleotide, and vice versa. Therefore, any sequence inherently has a 3' portion and a 5' portion. Even so, the sequences of Corey have 3' termini.

15. Claims 101, 107, 109, 111-119, and 123 are rejected under 35 U.S.C. 102(e) as being anticipated by Mayrand (US Patent; 5,691,146; 5/5/1995).

Mayrand discloses a composition comprising 3 oligonucleotides (a probe and 2 primers) and Taq polymerase (cleavage agent) in a buffer solution, wherein the probe is labeled with a fluorescent dye at it's 5' end, such as flourescein (charged adduct) (instant claims 101, 112, 113, 117-119; see abstract; col. 4, lines 37-50; and col. 9, lines 6-45). It is further noted that any of the nucleotides at the 5' end of any of the oligonucleotides can also be considered a "charged adduct" (claim 123). It is further noted that the teaching of a thermostable polymerase with 5' nuclease activity is inherently a teaching of the limitations in claims 107, 109, and 111. Further, Mayrand teaches a linker for the charged adduct (claim 116, see col. 8, lines 46-60). As the claims do not make clear that the first target and the second target are different, such teaching of more than one target in a reaction is interpreted to encompass instant claim 115.

Response to Arguments

16. The response traverses the rejection and asserts that Mayrand fails to teach reagents comprising first and second oligonucleotides that can anneal to contiguous regions of a target wherein the 2nd oligonucleotide further comprises a 3' portion. This argument has been thoroughly reviewed but was found unpersuasive. The claims only require that a target nucleic contain two contiguous regions, it is not limited to a structure where 2 oligonucleotides are

hybridized contiguous to each other, or to oligonucleotides that hybridize over a complete region of the target. Further, the term "region" is not specifically defined, and it is not clear how many nucleotides are necessary to define a "region" on the target. Two nucleotides side by side would encompass a first region contiguous to a second region. It should additionally be noted that the terms "3' portion", and "5' portion" have not been interpreted to be limited to 3' or 5' termini, respectively, of a molecule. A portion can be considered a 3' portion as long as it has something 5' to it, even a single nucleotide, and vice versa. Therefore, any sequence inherently has a 3' portion and a 5' portion. Even so, the sequences of Mayrand have 3' termini.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. No claims are allowable over the cited prior art.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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3/2/05